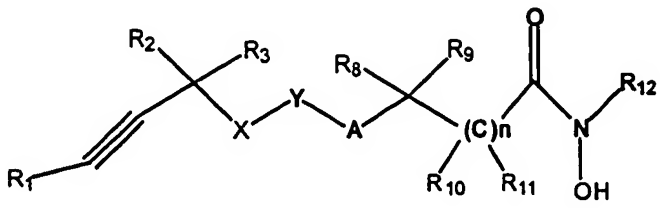
APPENDIX

AMENDMENTS TO THE CLAIMS

Please amend the claims as follows:

Claim 1 (currently amended). A compound of formula



wherein:

R_1 is hydrogen, aryl, heteroaryl, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, or C_5-C8-cycloheteroalkyl having from 1-2 heteroatoms selected from N, NR_7, S and O;

R_2 and R_3 are each independently, hydrogen, alkyl of 1-6 carbon atoms, -CN, or –CCH;

$R_5$is hydrogen, alkyl of 1-8 carbon atoms, cycloalkyl of 3-6 carbon atoms, aryl, heteroaryl, or C4-C8-cycloheteralkyl;

$R_7$is hydrogen, aryl, aralkyl, alkyl of 1-6 carbon atoms, or cycloalkyl of 3-6 carbon atoms, oxy, C1-C8 alkanoyl, $COOR_5$, COR_5, -SO_2-C1-C8 alkyl, -SO_2-aryl, -SO_2-heteroaryl, -CO-NHR_1;

R_8, R_9, R_{10}, and R_{11} are each, independently, hydrogen, aryl, aralkyl, 5-10 membered heteroaryl having from 1-3 heteroatoms selected from N, NR_7, O and S, heteroaralkyl having from 1-3 heteroatoms selected from N, NR_7, O and S, cycloalkyl of 3-6 carbon atoms, -C_4-C_8-cycloheteroalkyl having from 1-3 heteroatoms selected from N, NR_7, O and S, alkyl of 1-18 carbon atoms, alkenyl of 2-18 carbon atoms, alkynyl of 2-18 carbon atoms;

R_{12} is hydrogen, aryl or 5-10 membered heteroaryl having from 1-3 heteroatoms selected from N, NR_7, S and O, cycloalkyl of 3-6 carbon atoms, -C_5-C8-cycloheteroalkyl having from 1 to 2 heteroatoms selected from N, NR_7, S and O, or alkyl of 1-6 carbon atoms;

A is O, S, SO, SO_2, NR_7, or CH_2;

X is O, S, SO, SO_2, NR_7, or CH_2;

Y is ~~aryl or~~ heteroaryl, with the proviso that A and X are not bonded to adjacent atoms of Y ~~and with the further proviso that Y is not phenyl~~; and

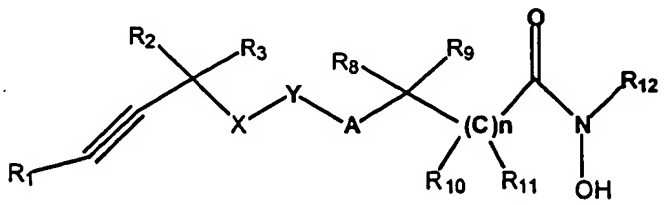
n is 0-2; or a pharmaceutically acceptable salt thereof.

Claim 2 (previously amended). A compound according to claim 1 wherein Y is pyridyl, thienyl, furanyl, imidazolyl, triazolyl, or thiadiazolyl.

Claim 3 (canceled).

Claim 4 (canceled).

Claim 5 (currently amended). A method of inhibiting pathological changes mediated by TNF-α converting enzyme (TACE) in a mammal in need thereof which comprises administering to said mammal a therapeutically effective amount of a compound having the formula:



wherein:

R_1 is hydrogen, aryl, heteroaryl, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, or C5-C8-cycloheteroalkyl having from 1-2 heteroatoms selected from N, NR_7, S and O;

R_2 and R_3 are each independently, hydrogen, alkyl of 1-6 carbon atoms, -CN, or –CCH;

$R_5$is hydrogen, alkyl of 1-8 carbon atoms, cycloalkyl of 3-6 carbon atoms, aryl, heteroaryl, or C4-C8-cycloheteralkyl;

$R_7$is hydrogen, aryl, aralkyl, alkyl of 1-6 carbon atoms, or cycloalkyl of 3-6 carbon atoms, oxy, C1-C8 alkanoyl, $COOR_5$, COR_5, -SO_2-C1-C8 alkyl, -SO_2-aryl, -SO_2-heteroaryl, -CO-NHR_1;

R_8, R_9, R_{10}, and R_{11} are each, independently, hydrogen, aryl, aralkyl, 5-10 membered heteroaryl having from 1-3 heteroatoms selected from N, NR7, O and S, heteroaralkyl having from 1-3 heteroatoms selected from N, NR_7, O and S, cycloalkyl of 3-6 carbon atoms, -C_4-C_8-cycloheteroalkyl having from 1-3 heteroatoms selected from N, NR_7,

O and S, alkyl of 1-18 carbon atoms, alkenyl of 2-18 carbon atoms, alkynyl of 2-18 carbon atoms;

R_{12} is hydrogen, aryl or 5-10 membered heteroaryl having from 1-3 heteroatoms selected from N, NR_7, S and O, cycloalkyl of 3-6 carbon atoms, -C5-C8-cycloheteroalkyl having from 1 to 2 heteroatoms selected from N, NR_7, S and O, or alkyl of 1-6 carbon atoms;

A is O, S, SO, SO_2, NR_7, or CH_2;

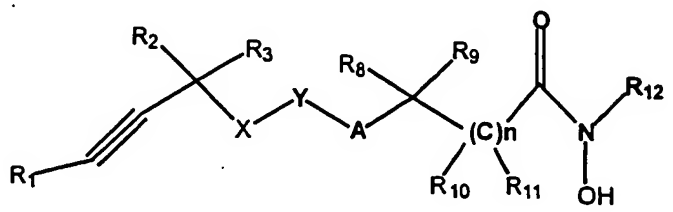
X is O, S, SO, SO_2, NR_7, or CH_2;

Y is ~~aryl or~~ heteroaryl, with the proviso that A and X are not bonded to adjacent atoms of Y ~~and with the further proviso that Y is not phenyl~~; and

n is 0-2; or a pharmaceutically acceptable salt thereof.

Claim 6 (original). The method of Claim 5 wherein the condition treated is rheumatoid arthritis, graft rejection, cachexia, inflammation, fever, insulin resistance, septic shock, congestive heart failure, inflammatory disease of the central nervous system, inflammatory bowel disease or HIV infection.

Claim 7 (currently amended). A pharmaceutical composition comprising a compound having the formula:



wherein:

R_1 is hydrogen, aryl, heteroaryl, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, or C5-C8-cycloheteroalkyl having from 1-2 heteroatoms selected from N, NR_7, S and O;

R_2 and R_3 are each independently, hydrogen, alkyl of 1-6 carbon atoms, -CN, or –CCH;

$R_5$is hydrogen, alkyl of 1-8 carbon atoms, cycloalkyl of 3-6 carbon atoms, aryl, heteroaryl, or C4-C8-cycloheteralkyl;

R_7 is hydrogen, aryl, aralkyl, alkyl of 1-6 carbon atoms, or cycloalkyl of 3-6 carbon atoms, oxy, C1-C8 alkanoyl, $COOR_5$, COR_5, $-SO_2$-C1-C8 alkyl, $-SO_2$-aryl, $-SO_2$-heteroaryl, -CO-NHR_1;

R_8, R_9, R_{10}, and R_{11} are each, independently, hydrogen, aryl, aralkyl, 5-10 membered heteroaryl having from 1-3 heteroatoms selected from N, NR7, O and S, heteroaralkyl having from 1-3 heteroatoms selected from N, NR_7, O and S, cycloalkyl of 3-6 carbon atoms, $-C_4$-C_8-cycloheteroalkyl having from 1-3 heteroatoms selected from N, NR_7, O and S, alkyl of 1-18 carbon atoms, alkenyl of 2-18 carbon atoms, alkynyl of 2-18 carbon atoms;

R_{12} is hydrogen, aryl or 5-10 membered heteroaryl having from 1-3 heteroatoms selected from N, NR7, S and O, cycloalkyl of 3-6 carbon atoms, $-C_5$-C8-cycloheteroalkyl having from 1 to 2 heteroatoms selected from N, NR_7, S and O, or alkyl of 1-6 carbon atoms;

A is O, S, SO, SO_2, NR_7, or CH_2;

X is O, S, SO, SO_2, NR_7, or CH_2;

Y is ~~aryl or~~ heteroaryl, with the proviso that A and X are not bonded to adjacent atoms of Y; ~~and with the further proviso that Y is not phenyl~~; and

n is 0-2; or a pharmaceutically acceptable salt thereof.